REMARKS

Claims 1, 4, and 7-24 are pending in the application. Claims 1 and 4 have been amended. Claims 2, 3, 5, 6, 25, and 26 have been canceled. Support for these amendments can be found in original claims 2 and 3 and in the specification at, e.g., page 4, lines 21-22; and page 15, line 30, to page 16, line 18. These amendments add no new matter.

Allowable Claims

At page 4 of the Office Action, the Examiner stated that claims 14 and 16 are dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. For the reasons presented herein, applicants respectfully submit that all of the currently pending claims are in condition for allowance and, therefore, no amendments to dependent claims 14 and 16 are required.

35 U.S.C. §103(a)

At pages 2-3 of the Office Action, the Examiner rejected claims 1-10, 15, 17-19, and 24 as allegedly unpatentable over Smith et al. (1998) *J. Exp. Med.* 188:17-27 ("Smith") in view of Huston et al., U.S. Patent No. 5,013,653 ("Huston") and Tudyka et al. (1997) *Protein Science*, 6:2180-87 ("Tudyka"). According to the Examiner,

> Applicants argue that the combined references do not offer a reasonable level of expectation of success. Applicants argue that Smith et al. merely predicts the transmembrane domain of SSAO and fails to demonstrate that a soluble and active SSAO could be produced. However, a skilled artisan would recognize that the transmembrane domain is anchoring the enzyme in the plasma membrane. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success of producing soluble SSAO by truncating the transmembrane domain.
>
> Applicants also that the present invention fuses the 3C protease substrate linker to amino acid no. 29 and not amino acid no. 28, the first residue following the transmembrane domain. Applicants list several reasons for this rationale. However, upon inspection of the amino acid sequence of SSAO, one of ordinary skill in the art would have also recognized the advantage of fusing the protease

linker at position no. 29 for reasons similar to the ones listed by applicants. As applicants have stated, there are numerous proteases in the cell and growth medium that cleaves at arginine residues. To ensure that the fusion partner and SSAO are not cleaved prematurely, it would have been obvious to add the linker at position 29.

Also, the examiner points out that the claims are drawn to any soluble fragments of SSAO and is not drawn solely on soluble SSAO consisting of residues 29-763 of SEQ ID NO:2.

Applicants respectfully traverse the rejection in view of the claim amendments and the following comments.

Claim 1 as amended is directed to a nucleic acid containing a nucleic acid that encodes a fusion protein consisting of: (i) a signal peptide; (ii) a soluble form of human semicarbazide-sensitive amine oxidase (SSAO) consisting of amino acids 29 to 763 of SEQ ID NO:2 or a fragment thereof exhibiting benzylamine oxidase activity; (iii) a fusion partner that enables dimerization of the soluble SSAO; (iv) a protease cleavage site; and (v) optionally one or more spacer amino acid sequences.

The cited references taken alone or in combination do not suggest a soluble SSAO fusion protein wherein the SSAO portion of the protein consists of amino acids 29 to 763 of SEQ ID NO:2 or a fragment thereof exhibiting benzylamine oxidase activity. In particular, the cited references lack a suggestion to exclude amino acid residue 28 of human SSAO from such a fusion protein.

Huston describes methods for the isolation and purification of polypeptides. However, nothing in Huston indicates how or even whether a SSAO protein can be modified to successfully obtain an active soluble protein. Huston makes no prediction as to the location of an SSAO transmembrane region and does not indicate what sequences of an SSAO protein should be included and/or excluded so as to generate a functional soluble protein. According to the nucleic acid of amended claim 1, a region of SSAO encompassing the transmembrane region as well as at least amino acid 28 have been deleted and replaced with a fusion partner that facilitates the dimerization of human SSAO monomers, thereby permitting the production of active SSAO.

In Smith, the transmembrane region of SSAO is predicted to extend from amino acids 5 to 27. Nothing in Smith suggests that amino acid residue 28 of human SSAO should be excluded from an SSAO fusion protein, as is required by the presently claimed invention. Smith provides the skilled artisan with no method that would have reasonably been expected to result in the production of a functional soluble SSAO fusion protein, much less a methodology that entails the exclusion of amino acid residue 28 of SSAO. Such a teaching is provided in the present application, but is lacking in the references of record.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the cited references or in the knowledge generally available to one of ordinary skill in the art, to modify a reference or to combine reference teachings to arrive at the claimed invention. In addition, there must be a reasonable expectation of success. The suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicants' disclosure. MPEP § 2143. In the present case, there is nothing in the references of record that would have led the skilled artisan to construct a secreted SSAO fusion protein wherein the SSAO portion of the protein lacks amino acid residue 28 and consists of amino acids 29 to 763 of SEQ ID NO:2 or a fragment thereof.

In light of these comments, applicants respectfully submit that the cited references do not render the claimed invention obvious and therefore request that the Examiner withdraw the rejection.

At page 3 of the Office Action, the Examiner rejected dependent claim 11 as allegedly unpatentable over Smith in view of Huston, Tudyka, and Zambidis et al., *Proc. Natl. Acad. Sci. USA*, 93:5019-24 (1996) ("Zambidis"). Zambidis was cited as describing a mouse IgG1 heavy chain signal peptide.

As detailed above, Smith, Huston, and Tudyka do not provide the skilled artisan with the requisite suggestion or motivation to combine and/or modify the reference teachings to result in the nucleic acid of amended claim 1. In addition, Zambidis's description of a signal peptide does not overcome the references' combined lack of suggestion to construct a secreted SSAO fusion

protein wherein the SSAO portion lacks amino acid position 28 and consists of amino acids 29 to 763 of SEQ ID NO:2 or a fragment thereof. For this reason, the combination of references fails to render obvious the nucleic acid of claim 1 as well as claim 11 that depends therefrom.

At page 4 of the Office Action, the Examiner rejected dependent claims 12, 13, and 20-23 as allegedly unpatentable over Smith in view of Huston, Tudyka, and Brenda Enzyme Database, EC 3.4.22.28 ("Brenda"). Brenda was cited in the present rejection as describing 3C protease amino acid sequences.

As detailed above, Smith, Huston, and Tudyka do not provide the skilled artisan with the requisite suggestion or motivation to combine and/or modify the reference teachings to arrive at the nucleic acid of amended claim 1. Brenda does not add what is lacking in these references. Brenda's description of 3C protease amino acid sequences does not overcome the references' lack of suggestion to construct a secreted SSAO fusion protein wherein the SSAO portion lacks amino acid position 28 and consists of amino acids 29 to 763 of SEQ ID NO:2 or a fragment thereof. For this reason, the combination of references fails to render obvious the nucleic acid of claim 1 as well as claims 12, 13, and 20-23 that depend therefrom.

Conclusions

Applicants ask that all claims be allowed in view of the amendments and remarks contained herein.

Please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 13425-053001.

Respectfully submitted,

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